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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/518,128

08/29/2005

Bronislava Gedulin

0402US-UTL

7370

44638 7590 02/03/2009

Intellectual Property Department
Amylin Pharmaceuticals, Inc.
9360 Towne Centre Drive
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EXAMINER

LI, RUIXIANG

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

02/03/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/518,128	Applicant(s) GEDULIN ET AL.	
	Examiner RUIXIANG LI	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5-12, 14-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 11/07/2008 has been entered. Claims 1-3, 5-12, and 14-32 are pending. Claims 1-3, 5, 6, 8-12, 14, and 22-32 are under consideration.

Withdrawn Objections and/or Rejections

The rejection of claims 1-3, 5, and 10 under 35 U.S.C. 103(a) as being unpatentable over El-Salhy et al. (Peptides 23:397-402, February 2002) is withdrawn in view of Applicants argument.

Continuing Data

The filing data of PCT/US03/18657 provided by Applicants in is not consistent with PTO records. The FORM PTO-1390 filed by Applicants on 12/14/2004 indicates that the international filing date of PCT/US03/18657 is April 24, 2003, whereas the PTO records indicate that the international filing date of PCT/US03/18657 is 06/13/2003. Moreover,

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the oath/Declaration filed on 08/29/2005 indicates that 10/518,128 was filed on December 14, 2004, whereas the PTO records indicate that the filing or 371(c) date of 10/518,128 is 08/29/2005.

Claim Rejections Under 35 U.S.C. §112, 1st Paragraph (New Matter)

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 1-3, 5, 6, 8-12, and 30-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claim 1 recites a limitation, “wherein said active fragment comprises amino acids 22-28 of the amino acid sequence set out in SEQ ID NO: 2”, which introduces new matter. There is no support for such a limitation in the application as filed.

Applicants argue that such active fragments consisting of amino acids 22-28, as well as multiple such active fragments comprising amino acids 22-28, were available in the prior art at the time of the priority filing date of the subject application. Citing MPEP 2163.07(b), Applicants argue that information incorporated is as much as a part of the

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application as filed as if the text was repeated in the application, and should be treated as part of the text of the application

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. Replacing the identified material incorporated by reference with the actual text is not new matter. See 37 CFR 1.57 and MPEP § 608.01(p) for Office policy regarding incorporation by reference. However, the material—"wherein said active fragment comprises amino acids 22-28 of the amino acid sequence set out in SEQ ID NO: 2" is not incorporated by reference and uniquely identified in the application as filed. Thus, it introduces new matter.

(iii). Claims 1-3, 5, 6, 8-12, and 22-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

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Claim 1 is drawn to a method of treating, ameliorating, preventing, or protecting from an intestinal damage, comprising administering a pharmaceutically active formulation of PYY or a PYY agonist to a human to treat, alleviate, or preventing the intestinal damage, wherein said PYY or said PYY agonist is a peptide that comprises an active fragment of PYY, wherein said active fragment comprises amino acids 22-28 of the amino acid sequence set in SEQ ID NO: 2. Claims 2, 3, 5, 6, 8-12, and 22-32 depend from claim 1. Thus, the claims are drawn to a method comprising administration of PYY or a genus of PYY agonists comprising amino acids 22-28 of the amino acid sequence set forth in SEQ ID NO: 2.

The specification defines PYY as a peptide YY polypeptide obtained or derived from any species, and defines PYY agonist as any compound which elicits an effect of PYY to protect from or reduce colon injury associated with inflammatory bowel disease or ulcerative colities *and* which binds specifically in a Y receptor assay or in a competitive binding assay (page 10). The specification discloses an actual reduction to practice and the complete chemical structure of only one species of the claimed genus of PYY agonists, i.e., PYY(3-36). The specification does not indicate that any other PYY agonists comprises amino acids 22-28 of the amino acid sequence set in SEQ ID NO: 2 that both protect from or reduce colon injury associated with inflammatory bowel disease or ulcerative colities and bind specifically in a Y receptor assay or in a competitive binding assay. The prior art does not teach the genus of PYY agonists in the context of the instant application.

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While claim 1 requires that a PYY peptide agonist comprises amino acids 22-28 of the amino acid sequence set forth in SEQ ID NO: 2, the specification does not disclose that the amino acids 22-28 of SEQ ID NO: 2 is critical (required) for the PYY agonist activity. Without a recognized correlation between structure and the defined function (page 10 of the instant specification), those of ordinary skill in the art would not be able to identify without further testing which of those peptides that comprise amino acids 22-28 of the amino acid sequence set forth in SEQ ID NO: 2 would also protect from or reduce colon injury associated with inflammatory bowel disease or ulcerative colitis and bind specifically in a Y receptor assay or in a competitive binding assay. Thus, those of ordinary skill in the art would not consider that Applicants were in possession of the encompassed genus of PYY agonists at the time the application was filed based on the single species PYY(3-36) disclosed.

Accordingly, the specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claim 1 and its dependent claims.

Response to Applicants' argument

At page 11 of Applicants' response, Applicants argue that the newly recited limitation, "wherein said active fragment comprises amino acids 22-28 of the amino acid sequence set in SEQ ID NO: 2", is demonstrated in the prior art. Applicants argue that representative active fragments of the PYY are disclosed in the prior art. Applicants

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further argue that the genus of active fragments of PYY, as recited in the claims, is adequately described in the instant application in the context to that which was known in the art at the time of the priority date of the subject application. Applicants' argument has been fully considered, but is not deemed to be persuasive for the reasons set forth immediately above.

(iv). Claims 1-3, 5, 6, 8-12, and 30-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating, ameliorating, or protecting from an intestinal damage, comprising peripherally administering a pharmaceutically active formulation of PYY or PYY(3-36) to a human to treat or alleviate the intestinal damage, does not reasonably provide enablement for the claimed invention commensurate in scope with the claims (see below). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

The factors considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8

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USPQ 2d 1400 (Fed. Cir. 1988).

Claim 1 is drawn to a method of treating, ameliorating, preventing, or protecting from an intestinal damage, comprising administering a pharmaceutically active formulation of PYY or a PYY agonist to a human to treat, alleviate, or preventing the intestinal damage, wherein said PYY or said PYY agonist is a peptide that comprises an active fragment of PYY, wherein said active fragment comprises amino acids 22-28 of the amino acid sequence set in SEQ ID NO: 2. Claims 2, 3, 5, 6, 8-12, and 22-32 depend from claim 1. The claims are broad because they are drawn to a method comprising administration of PYY or a genus of PYY agonists comprising amino acids 22-28 of the amino acid sequence set forth in SEQ ID NO: 2. The claims not only encompass a method of treating an intestinal damage, but also preventing an intestinal damage; the method not only encompasses a method of peripherally administering a pharmaceutically active formulation of PYY or PYY(3-36) to a human, but also encompass a method of centrally administering a pharmaceutically active formulation of PYY or PYY(3-36) to a human.

The specification discloses that reduction of colon injury of animal model for inflammatory bowel disease by peripheral administration of PYY(3-36) (Example 1; page 7, the 3rd paragraph). However, the specification does not provide guidance and working examples with respect to *preventing* an intestinal damage by administering PYY or a PYY agonist or treating an intestinal damage by *centrally* administering PYY

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or a PYY agonist. Moreover, the specification fails to provide sufficient guidance and working examples on how to make and use the genus of PYY agonists. The specification does not disclose that the amino acids 22-28 of SE! ID NO: 2 are critical for the PYY agonist activity defined in the instant specification. While the prior art teaches PYY agonists (e.g., US patent No. 5,912,227, 5,916,869, 6,017,879, WO 03/026591), they are not taught in the same context of protecting from or reducing colon injury associated with inflammatory bowel disease or ulcerative colities and binding specifically in a Y receptor assay or in a competitive binding assay..

The prior art teaches treating gastrointestinal disorders that are associated with excess intestinal electrolyte and water secretion as well as decreased absorption, such as infectious or inflammatory diarrhea, or diarrhea resulting from surgery comprising administering to a human a pharmaceutical formulation comprising PYY (Balasubramaniam, US Patent No. 5,604,203, Feb. 18, 1997). The prior art also teaches that peripheral administration of PYY or PYY(3-36) inhibits pancreatic exocrine and gastric acid output in mongrel dogs (Yoshinaga et al., *Am. J. Physiol.* 263:G695-701, 1992), reduces body weight in 12-week-old mice (Morley et al., *Life Sci.* 41:2157-2165, 1987).

In view of the complexity of the nature of PYY-related compounds, it is unpredictable whether a compound that is related to PYY would work in the same manner as that of PYY. Therefore, it would require undue experimentation for one skilled in the art to

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make and/or use the invention commensurate in scope with the claims.

Claim Rejections Under 35 U.S.C. §102 (b)

(i). The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(ii). Claims 1, 2, 5, 10-12, and 22-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Balasubramaniam (U. S. Patent No. 5,604,203, Feb. 18, 1997).

Balasubramaniam teaches PYY and a pharmaceutical formulation comprising PYY (columns 15-16). The human PYY comprises amino acids 22-28 of SEQ ID NO: 2 of the present invention and the amino acid residues recited in claims 23-29 (column 2). Balasubramaniam teaches treating gastrointestinal disorders that are associated with excess intestinal electrolyte and water secretion as well as decreased absorption, such as infectious or inflammatory diarrhea, or diarrhea resulting from surgery (column 16) comprising administering to a mammal, such as a human (column 6, lines 43-47). Inflammatory diarrhea includes Crohn's disease (column 7), a form of inflammatory bowel disease. The intestinal damage caused by these gastrointestinal disorders necessarily comprises a morphological damage, such as those listed in claims 30-32.

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Balasubramaniam also teaches that PYY inhibits gut motility and blood flow, attenuates basal and secretagogue-induced intestinal secretion in humans. Balasubramaniam further teaches that PYY plays a physiological role in regulating intestinal secretion and absorption, serving as natural inhibitors of diarrhea (column 1, lines 35-54; column 6, lines 43-67). Balasubramaniam further teaches that the compounds can be administered orally or parenterally (intravenously or subcutaneously) (column 14). The daily dose in the case of oral administration is typically in the range of 0.1 to 100 mg/kg body weight, and the daily dose in the case of parenteral administration is typically in the range of 0.001 to 50 mg/kg body weight (column 16).

Accordingly, the teachings of Balasubramaniam meet the limitations of claims 1, 2, 5, 10-12, and 22-32.

Response to Applicants' argument

Applicants argue that the reference provides no nexus between the alleged teaching of treating recited disorders and treating, ameliorating, preventing, or protecting from intestinal damage that is inflicted on a subject as a result of experiencing such disorders. Applicants argue that the claims have been amended to recite that the recited intestinal damage comprises a morphological damage. Applicants argue that the cited reference is clearly and absolutely silent with regard to treating, ameliorating, preventing, or protecting from intestinal damage that comprises, for example, morphological damage. Applicants argue that the cited prior art does not disclose each and every element of the present claims, and therefore does not anticipate the instant

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claims. Applicants' argument has been fully considered, but is not deemed to be persuasive for the reasons set forth immediately above.

Claim Rejections Under 35 U.S.C. §103 (a)

(i). The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

(ii). Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Balasubramaniam (U. S. Patent No. 5,604,203, Feb. 18, 1997), as applied to claims 1, 2, 5, 10-12, and 22-32 above, and further in view of Dumont et al. (Brain Res. Mol. Brain Res. 26: 320-324, 1994).

Balasubramaniam teaches a method of treating an intestinal damage comprising administering a pharmaceutically active formulation of PYY to a human subject as applied to claims 1, 2, 5, 10-12, and 22-32 above.

Balasubramaniam fails to teach the method of claim 14, comprising administering PYY[3-36].

Dumont et al. teach a PYY agonist, PYY[3-36] that binds PYY receptors (see Abstract).

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Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use PYY[3-36] in the method of treating a gastrointestinal disorder, such as Crohn's disease (a form of inflammatory bowel) as taught by Balasubramaniam with a reasonable expectation of success. One would have been motivated to do so because Balasubramaniam teaches PYY and PYY functional analogs can be used to treat a gastrointestinal disorder, such as Crohn's disease (first paragraph of column 7), whereas PYY [3-36] that binds to PYY receptors is expected to have the similar effect in treating a gastrointestinal disorder, such as Crohn's disease.

Response to Applicants' argument

Applicants argue that Balasubramaniam fail to teach a method of treating intestinal damage comprising administering a pharmaceutically active of PYY or a PYY agonist polypeptide as instantly claimed. Applicants argue that Dumont may teach that a PYY agonist, PYY [3-36], binds PYY receptors, but fails to cure the deficiencies of the teachings of Balasubramaniam. Applicants' argument has been fully considered, but is not deemed to be persuasive for the reasons set forth above.

Claim Rejections under 35 USC § 112, 2nd paragraph

(i). The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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(ii). Claims 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 is indefinite because it recites one limitation "wherein said active fragment comprises an amino acid sequence as set out in SEQ ID NO: 2", which is contradicting to another limitation "wherein said fragment comprises a deletion of about 5 amino acids from the N-terminus of said amino acid as set out in SEQ ID NO: 2". Claims 28 and 29 are indefinite for the similar reasons.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/

Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.

January 30, 2009